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GENETICS

MODERN EMBRYOLOGY ON THE ROAD TO GENETIC ENGINEERING IN ANIMALS

Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA in Russian No 3, 1978 pp 36-44

[Article by K.G. Gazaryan and A.A. Yazykov, Department of Embryology, Moscow University]

[Text] At the present time, we are more acutely aware of the need to utilize breakthroughs in basic biology to solve applied problems. For example, genetic engineering of bacteria promises in the near future to change fundamentally the technology utilized in the microbiological industry. However, significantly more important practical problems, which require solution, are connected to discovery of methods to alter the genotype of higher organisms, such as plants, animals, and man. Current methods of genetic engineering used on bacteria as yet cannot be directly applied to these higher organisms; nevertheless, individual attempts to introduce genetic material in somatic cells of higher organisms have already been carried out (Aposhian, 1970; Qaspa, Aposhian, 1971). A more general approach to genetic engineering in higher organisms is outlined in the current methods of experimental embryology. These methods are similar to those used in the fields of molecular biology and molecular genetics, in which there have already been significant achievements in understanding the structure and function of the genetic apparatus. Experimental embryology has been concerned for a long time with explaining the interrelationship and interdependency between the formation of separate components which comprise a developing organism--the multi-cellular phase of growth. Currently, embryologists have directed more attention to the period of development when an organism is represented by a monocellular phase--the reproductive cell. Based on comprehension of the fundamental importance of this stage in the development of multicellular organisms, it has become increasingly more evident that one potentially succesful mode of intervention in

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the genome of animals will be through the ovum.

Embryologists have already begun to manipulate ova and nuclei of somatic cells in animals. Research on transplantation of the nucleus, done over the past 40 years, has led to the elaboration of precise methods for surgery on individual cells. Successful experiments to enucleate ova of amphibians (Porter, 1939) and experiments to develop techniques for nuclear transplantation (Lopashov, 1945) provided the foundation for expansion of research in this direction. These experiments initially led scientists to conclude that in order to understand the mechanism of cell differentiation in individual organs and tissues of an organism, they would have to explain the genetic changes which occur in the nuclei of cells formed by differentiated ova in a multicellular organism. In 1952, the genetic potential of the nuclei of frog blastule cells was successfully tested by transplanting them in enucleated ova. These ova, which contained the nuclei of somatic cells of early embryos, developed into normal frog larvae. Thus, by using egg cytoplasm, it was possible to restimulate the nuclei of several blastule cells which subsequently proved to be genetically capable of accomplishing normal development (Briggs, King, 1952). Recently, these experiments to reprogram the somatic nuclei by using ova have stimulated a series of studies in different laboratories. The continuing efforts of embryologists have been directed at working out new research techniques, selecting new models, analyzing cell nuclei which pertain to various organs, and explaining the molecular-biologic basis for the reprogram process. Presently, by transplanting nuclei to ova, scientists have succeeded, to varying degrees, in reprogramming the genome of somatic cells in at least nine amphibian species (Briggs, King, 1952; Lehman, 1955; Stroyeva, Nikitina, 1960; Gurdon 1962b; Sládeček, Mazáková-Štefanová, 1964; Subtelny, 1965; Nikitina, 1969; and others), in one insect species (drosophila) (Illmensee, 1969), and just recently, in one type of bony fish (loach) (King, Gazaryan, 1978).

Even as early as 1957, scientists understood that, depending on the extent of cell differentiation during embryogenesis, the number of nuclei, which after transplantation to the ova could assure development, decreased. The more advanced the embryonic stage to which the cell is connected--the nucleus donor-- the earlier the development of the functioning ovum can be interrupted. In a majority of cases, development of such ova was halted at one of the intermediate stages: from the beginning of subdivision to the larval stage (Briggs, King, 1957). Similar results were obtained in a number of recent studies. Gurdon (Gurdon et. al., 1958) was the first scientist to obtain grown spur frogs from ova in which somatic cell nuclei, taken from embryos at different stages of growth, were transplanted. Soon after Gurdon's

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work was reported, a paper appeared which described obtaining mature frogs from ova with nuclei taken from intestinal cells of amphibious larvae (Gurdon, 1962b). Somewhat latter, it was shown that ova with nuclei transplanted from the intestines of amphibian larvae could develop into sexually mature and fertile specimens(Gurdon,Uehlinger, 1966). At the same time, in experiments to achieve interspecies transplantation of nuclei in amphibians, nuclear-cytoplasmic hybrids were grown which reached the early stages of development (Moore, 1958; Gurdon, 1962a). The important achievements of work in transplantation of somatic nuclei in enucleated ova has broad application to mass production of transplanted nuclei used in cloning techniques. Animals with the same genotype can be obtained by cloning, i.e. genetic copies of one species. The genetic identity of such animals was confirmed by cross-transplantation of skin sections to test tissue compatibility (Simnett, 1964). Transplanation of nuclei from cells of mature donors was accomplished in 1966: nuclei from frog liver, brain and blood cells, and mouse liver cells were transplanted in enucleated frog ova. These ova did not develop but the inception of DNA synthesis was recorded in them (Graham et.al., 1966). Subsequently, this line of research was also successful in our country. Kidney, lung, and skin cells were placed in culture, and then were used as nuclei donors. As a result, in 5-12 percent of cases, amphibian larvae were obtained. Histological analysis of the larvae did not disclose deviation from the norm. The basic theoretical conclusion drawn from these studies was that cells of designated tissues from a mature vertebrate animal contain nuclei which can be reprogrammed in ova and can assure the development of all other tissues and organs, at least until the larval stage (Laskey, Gurdon, 1970). Just recently, it was successfully demonstrated that nuclei from such highly differentiated (specific for the synthesis of keratin) cells as those from the webbed f t of mature frogs can be reprogrammed and can produce normal larvae (Gurdon, et.al., 1975). This line of research indicated that the cytoplasm of an ovum is capable of altering the function of a nucleus, which had previously undergone normal differentiation. It has been suggested by researchers that the cytoplasm of an ovum acts to normalize the function of nuclei, subject to mutation or cancerous regeneration. Nuclei from adenocarcinomatous frog cells were transplanted in normal frog ova. As a result, normal embryos were obtained and normal amphibian larvae developed (MacKinnel et.al., 1969). Cytoplasm from ova of a normal species of frog +/+ was injected into ova of °/° mutant axolotl, which in normal conditions develop only to the gastrula stage. By this process, it was possible to partially correct the genetic defects--the mutated ova acquired the ability to develop to the stage of amphibian larvae (Briggs, Gustus, 1968). In mutant species of drosophila, researchers partially

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corrected the genetic disturbances (Okada, et.al., 1974). Based on advances in research on amphibians, scientists are conducting studies to perform similar work on mammalian ova. However, for this model, it was necessary to overcome large numbers of technical problems, arising from the small dimensions of the egg (in amphibians an ovum is 1-2 mm, in mammals; in mice ~ 70 µM, in rabbits ~ 100 µM, in man ~150 µM) and the specifics of intrauterine development. Progress in this direction was made possible by the development of relatively simple and standardized methods for culturing, in synthetic media, of mammalian ova and embryos inside an organism (Purshoftan, Pincus, 1961; Brinster, 1963; New, Stein, 1964; Daniel, 1971). Also a reliable technique has been worked out for transplanting early embryos in an organism of an "adopted mother" where their development is then completed normally. These systematic methods made possible earlier embryonic development in mammals by allowing direct observation of the complete life cycle and use of the most varied kinds of experimental intervention. Tarkowski (Tarkowski, 1961) suggested a method for joining two early embryonic mice. Utilizing this method, Mintz obtained more than 1,000 genetically mosaic mice (allophenic mice), the tissues of which came from cells of two different genotypes. Work with allophenic mice was based on current clonal theories of organ and tissue development (Mintz, 1970). Experiments using surgical procedures on mammalian ova were shown to be significantly more difficult. Such operations required use of special apparatus and experienced handling of microsurgical techniques. In 1966, Lin (Lin, 1966), using the appropriate instruments, injected mouse ova with beef gamma-globulin. The ova, after brief cultivation in artifical media, were transplanted into the uterus of a mouse which subsequently delivered a normal offspring. Soon after, Lin (Lin, 1967) successfully extracted part of the cytoplasm from a fertilized mouse ovum without harming its viability. After these studies, Lin became interested in the possibility of conducting experiments not only on embryos, but also on mammalian ova. In 1975, surgical removal of one pronucleus from a fertilized mouse ovum was accomplished. Haploid embryos which had reached the 50-cell stage were obtained (Modlinski, 1975).

In the same year, Bromhall (Bromhall, 1975) succeeded by both surgical and viral means in transplanting the nucleus of a somatic cell from an early rabbit embryo (a morula) to an ovum. The transplantation was conducted without removing the nucleus from the ovum recipient. Performing approximately 700 complex operations, Bromhall observed that four spontaneously enucleated ova developed normally and reached the 18-26 cellular stage. After these experiments, scientists concluded that transplantation of a somatic nucleus into an enucleated mammalian ovum had been successfully accomplished, evidenced by the resulting de-

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velopment of an early rabbit embryo. Currently, experiments on mammalian eggs are being conducted on the same methodologic level used on amphibians. It is evident that the development of surgical techniques appropriate for ova of laboratory mammals will be an important step towards possible transplantation of ova in agricultural animals and perhaps in man.

This series of experiments in embryology served as the foundation of one of the most important theories in modern biology. This theory asserts that a complete assembly of genes, required for the construction of the entire organism, is contained in the somatic cell of a multicellular organism. The genetic program, contained in one somatic cell can be completely or partially realized with the aid of the cytoplasm of the ovum. In essence, this conclusion opens up new approaches to genetic engineering in animals.

Two circumstances which have become practical reality in the present day promise to sharply accelerate work to produce the technology needed to perform genetic engineering in animals. One is the wide spread application of basic advances in molecular biology and molecular genetics, and the other is the development of precision techniques, based on modern instrument technology.

The problem facing modern genetic engineering, no matter to which subject it is applied, is comprised of two basic components: 1) chemical enzymatic manipulation with DNA for the purpose of obtaining recombinant molecules and 2) selection of a "vector" system which effects their introduction and integration into the genetic apparatus.

This same complex of methods required to obtain recombinant molecules apparently can be applied to both a pro- and a eukariotic system. However, the limitations of their applicability to one or another organism depends on the actual effectiveness of the selected "vectors". Such limits are presently recognized and these methods are used primarily for bacteria (Bayev, 1976). It is still not entirely clear which will be the best vectors to introduce elements into the genetic apparatus found in ova and eukariotic cells.

Based on the studies mentioned above, it is doubtful whether the central mission of future genetic engineering in higher organisms will be based solely on further understanding of the ovum. At the present time, the ovum is the only monocellular component during the formation of a multicellular organism through which, by utilizing genetic engineering methods, one can effectively influence the structure and genetic properties of an organism. Other suitable vectors are still unknown. This search

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for vectors has led to experiments where animal ova were injected with informational macromolecules, the components of the transcriptional and translational apparatus. The ova were injected with DNA, RNA, structural proteins and enzymes, regulatory proteins, ribosomes and mitochondria; that is, any structural element of the cytoplasm and nucleus capable of influencing in one way or another the characteristics of the future species. It is particularly interesting to introduce components which could produce a stable and specific influence on the reproductive apparatus; DNA is such a component. Previously, studies conducted in many laboratories to effect transformation in animals by means of injecting DNA into a growing organism proved to be unsuccessful. Experiments of direct or indirect introduction of DNA into ova were significantly more promising. Successes were achieved only in experiments with insects. In a series of studies, carried out in Fox's laboratory (Fox, Yoon, 1966; Fox, et. al., 1971) it was clearly demonstrated that when drosophila eggs were injected with DNA, the latter penetrates them and appears to be included in their genetic information. Authors came to the conclusion that the integration of DNA into a gene does not occur like the typical process of transformation. Recently a report appeared about injection of DNA inside an egg (Germeraad, 1976). Judging from the results, the injection was significantly more effective in this experimental arrangement because DNA was integrated into the gene. It is now clear that the technical obstacles have been essentially overcome in experiments with insects. Evidently, in the near future, we can expect successful transformation from experiments where DNA is injected into ova of other animals.

Following this work, it has been clearly shown that mRNA from different animals (for example, rabbits and mice) can be introduced into the oocyte of amphibians and that this RNA is translated for a prolonged time (Gurdon, et.al., 1973), forming complete proteins. This resolved a very important question: the translation apparatus in higher organisms does not possess a high degree of specificity and can be artifically combined with mRNA, ribosomes, and translation factors from other, entirely unrelated forms. Just recently, experiments were conducted to introduce foreign mRNA into ova (Woodland, et.al., 1974). It was shown that mRNA in rabbit hemoglobin, when injected in large amounts into a frog egg does not impede the egg's development and is actively translated in differentiated and mitotic cells of an embryo. Evidently, in the near future, we can expect the introduction in ova of mRNA, an active substance which may enter into specific structures or functionally interact with components of differentiated cells. Considering that foreign mRNA is not broken down in embryonic cells, one can expect a stable manifestation of its effect for a significant period of embryonic development.

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Experiments to introduce proteins into ova are still limited and are preliminary in nature. We also expect interesting results from this work. The introduction of proteins which serve as functional regulators of genetic activity (histones, nonhistones, proteins, RNA polymerase etc.) may alter dominant genes during the course of early embryogenesis.

One of the most significant results from these series of experiments on ova is the conclusion that an ovum is capable of retaining its potential for growth and formation of a complete multicellular organism after quite appreciable interference with its strcture, to the extent of replacing the elements of its genetic apparatus. It is still not entirely clear how far one can go in altering the structures and organization of ova, but it is already apparent that nature does impose some formidable limits on this, providing the ovum with both the ability to resist these influences and with the ability for self regulation.

We now turn our attention to several of the most important basic and applied aspects of developments in the field of genetic engineering in ova.

Presently, great success has been achieved in research on the molecular organization and structure of the genetic apparatus of the eukaryote. The structure of many proteins has been studied in depth, the sequence of RNA nucleotides has been successfully decoded and the sites for individual genomes appreciated. Many protein and nucleotide components of the nucleus and cytoplasm are now understood. These components participate in the mechanisms for storing,interpreting, transfering, and realizing reproductive information. While significant progress has been made in structural understanding, very little is known about the concrete function of the macromolecules which form the basis of the genetic apparatus of a eukaryote (histones, nonhistone proteins repeated in the DNA sequence, "redundancies" in the DNA sequence, heterogeneous nuclear RNA and others). At this time, the fundamental principles of gene function (recessive, dominant) in the organisms they determine remain unknown. Also, it is unclear whether genes act on their analogues as genetic regulators, inhibitors, or promotors. By experiments on bacteria, researchers are now beginning to understand the function of different components in the genetic apparatus of prokaryotic analogues. Apparently, because the characteristics of the eukaryotic system (the diploid genome, characterized by a double set of chromosomes in somatic cells, split between transcription and translation functions and other arrangements) complicate the mechanism of gene experession in higher organisms, the genetic-physiologic approach to understanding the mechanism for gene expression in bacterial

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cells (a prokaryotic system) is not as effective when applied to multicellular organisms. Thus, new approaches are required to study the eukaryotic system. Further elaboration and improvement of genetic engineering methods in ova will allow scientists to trace in detail the function of genetic substances which are introduced in oocyte structures. Also, scientists foresee the elaboration of effective and precise methods for replacement of the internal structures of mammalian ova from which an embryo develops. The ovum is a convenient test system for study of the structural components of the genetic apparatus and the potential and latent reserve of genetic resources found in them. Utilizing this approach, scientists may be able to trace how externally introduced components are integrated into the genetic apparatus of the recipient, how they interact with its components, how they are transmitted to daughter cells in the course of cellular division, and what impact this will have on the viability of the mature specimen. Thus, genetic engineering of ova opens up broad possibilities for investigation into the function of components in the genetic apparatus of higher vertebrate animals. The extensive study of the elements which make up the genetic apparatus in ova aids in understanding which components appear to possess "vector" properties. One can assume that viruses and mitochondria will prove to have "vector" properties. Ribosomal genes have not been ruled out as vectors nor have repeated sequences of DNA. Injection of viruses into ova--a highly promising way to identify which elements are candidates for vectors--will aid in selection and then introduction of non-pathogenic (or weakly pathogenic) viruses into the genome of forming tissues and organs. Based on the selective character of the virus-cellular relationship, it is possible to transfer genes to different tissues by this method. The mitochondria of a eukaryote, the genome of which has relatively small dimensions and is not too different in organization from the DNA of bacterial plasmid, can become a good object for application of genetic engineering techniques. Reproduction of the mitochondria is relatively automatic by the nucleus and they can be propagated and transferred to a number of generations of tissue and organ cells. The process by which the mitochondrial genome is expressed provides a good way to study the general process of genome integration of the nucleus because the mitochondria lack histones which are capable of nonspecifically suppressing the activity of the genes.

Research on transplantation of the nucleus from cancerous cells to an ovum (McKinnel, et.al., 1969) and fusion of cancerous cells with early embryos (Mintz, Illmensee, 1975) present extremely interesting possibilities. In similar experiments, different forms of cancerous cells are being tested to ascertain the reversibility of nonreversibility of changes which occur in their genetic apparatus.

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If recent progress in the field of transplantation of somatic nuclei to ova of warm-blooded animals is continued successfully, then genetic copies of higher organisms will give modern experimental medicine unique models for solutions to therapeutic, immunologic and behavior problems. The resulting genetic copies of agricultural animals will allow retention and propagation of rare genetic qualities, useful for man.

Thus, experimental embryology has already been used to solve some of the fundamental and applied problems which face modern biology.

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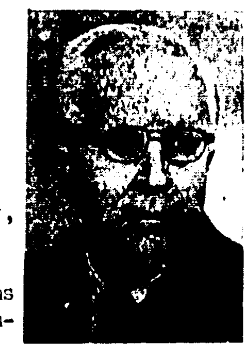
SCIENTISTS AND SCIENTIFIC ORGANIZATIONS

AWARDING OF GOLD MEDALS AND PRIZES OF THE USSR ACADEMY OF SCIENCES

Moscow VESTNIK AKADEMII NAUK SSSR in Russian No 11, 1978 pp 139-140

[Text] **Gold Medal imeni I. I. Mechnikov to M. S. Gilyarov.** The Presidium of the Academy of Sciences of the USSR has awarded the Gold Medal imeni I. I. Mechnikov for 1978 to Academician Merkuriy Sergeyevich GILYAROV for a series of papers on the problem "Patterns and Directions of Phylogenesis."



Academician M. S. Gilyarov is one of the greatest specialists in the field of evolutionary morphology, phylogenetics, taxonomy and ecology.

The series that earned the medal deals with problems of the evolution of terrestrial invertebrates. Comparative analysis of materials obtained in recent decades -- not only on the morphology of invertebrates on different stages of their ontogenesis, but also on their physiology, biochemistry, ecology and ethology -- enables understanding of the paths of evolution of invertebrates that are associated with the change of habitats in the course of phylogenesis. With a transition from an aqueous mode of life through habitation in soil and similar substrates to life on the surface of dry land, convergent changes of organization have taken place in organization in different phylogenetic branches of invertebrates. These changes are determined by general features of organization previously worked out, and by the principles of maximum effectiveness of basic functions under the new conditions of the environment.

M. S. Gilyarov examined changes in coverings, the respiratory system, the excretory system, paths of protein and purine catabolism, methods of insemination and other peculiarities of representatives of different groups of terrestrial arthropods that belong to different phylogenetic branches. He showed that the process of phylogenetic changes with the transition to life on dry land is characterized by a definite direction of the changes in organs and may be evaluated as regular. The course of phylogenesis is directed by changes in relations with the environment and is regulated by the feedback principle.

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Prize imeni I. I. Mechnikov to R. V. Petrov. The Presidium of the Academy of Sciences of the USSR has awarded the Prize imeni I. I. Mechnikov for 1978 in the amount of 2000 rubles to Member of the Academy of Medical Sciences of the USSR Rem Viktorovich PETROV (Institute of Biophysics of the Ministry of Public Health of the USSR) for the monograph "Immunology and Immunogenetics."

Rem Viktorovich Petrov deals with the most topical issues of immunogenetics, incompatibility of genetically differing tissues (transplantation immunogenetics) and the genetics of antibody genesis.

The monograph "Immunology and Immunogenetics" sheds light on the current state of theoretical immunology and its application to clinical practice. The book examines the T- and B-systems of immunity, lymphocyte receptors, interactions of cells in immune reactions, mechanisms of transplantation immunity, immunological tolerance, genetic control of the immune response, the concept of immunological supervision and other problems. The book gives special attention to those aspects of modern theoretical and experimental immunology that actually may have (or already do have) practical value. Of considerable interest from this standpoint are the divisions of the book that deal with functional evaluation of the T- and B-systems of lymphocytes in clinical practice, with inborn anomalies (immunodeficits) in children, autoimmune disorders, immunology and immunogenetics of tumors, immunodepression therapy.

The author of the book and his coworkers have made a great contribution to the elaboration of such problems as the interaction of trunk cells with lymphocytes, genetic control of the immune response against leptospires and against sheep erythrocytes, immunology of cellular chimerism, inborn immunodeficits, the immune response in aging.

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SCIENTISTS AND SCIENTIFIC ORGANIZATIONS

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REFERENCE AND BIBLIOGRAPHIC-ABSTRACT PUBLICATIONS OF SCIENTIFIC RESEARCH INSTITUTES SPECIALIZING IN BIOLOGY (A SURVEY)

Moscow NAUCHNO-TEKHNICHESKAYA INFORMATSIYA in Russian No 10, 1978 pp 21-27

[Article by G. S. Yukova and G. S. Lozovskaya, submitted 20 Jul 77]

[Text] The information publications of scientific research institutes specializing in biology under the USSR Academy of Sciences and academies of Union republics are usually represented by reference books, bibliographic and abstract collections. All these publications are printed in few copies and have limited distribution. Nevertheless, they are very important to institutes, since they cover and actively disseminate the main achievements in scientific research conducted at the institutes, they aid in coordinating research and establishing scientific contacts. Reference and information books are mainly departmental. The contents of such publications are directly related to the activities of the corresponding institutions [1].

In this work, we shall discuss only reference-information and bibliographic-abstract publications of biological institutes. There are no standardized rules on compilation of such information publications. We have directed ourselves more to drawing attention to the publications, to demonstrate their importance and timeliness, rather than generalization of the knowhow in publication of information collections by some biological scientific research institutes, singling out their main structural and meaningful elements, definition of their functional and goal-oriented purpose.

Development of standard plans for making up information publications of the same type (optimization and unification of their structure) plays an important role in refining information publications. The starting point is to classify the information publications, and this is based on analysis of the flows of original sources that are processed, methods of processing them, subject [goal] orientation and area of application of the information publications [2]. The lack of unified specifications with respect to the structure of reference and information editions results in loss of necessary information and unwarranted increase in size of the publications.

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Reference Books

Several biological institutes (Table 1) have published reference books [3-21], in which information is given about the structure, scientific personnel, scientific research and scientific organizational activities of institutes. These publications have different titles: "Reference Book," "Brief Information," "Prospectus--Reference Book," "Prospectus." In some of the books, the type of publication is not indicated, either in the title or introduction [6, 7, 9-12, 17-19]. This compels bibliographers to add explanatory words to the bibliographic description, for example, "essay." The inaccuracy of the bibliographic description makes it difficult to search for publications.

Information publications are a means of communication between specialists of similar and related branches of science, a sort of guide book for institutes. Since a reference book should make it easier for scientists visiting from other countries to become acquainted with an institute and it should aid in establishing contacts, it would be reasonable to publish reference books in several languages and at least two. For example, the reference books of the Institute of Protein and Institute of Developmental Biology are published in Russian and English [22, 23]. The annual of the Laboratory of Molecular Biology (Italy) [24], in which information reflected in domestic reference books is included along with abstracted information, is published in two languages also.

Reference books in which there is a separate heading indicating the address of the institute, complete name, surname and patronymic of management personnel and their business telephone numbers are given are the most convenient for users of information. Exclusion of such information from reference books, as was done in publications of several institutes [17, 19], minimizes the communicative value thereof.

Information about the scientific personnel of institutes is particularly important. It offers an idea about the scientific manpower and scientific potential of an institute. It must be noted that the roster of scientific personnel of an institute is of interest not only to scientific personnel of other institutes, but information workers dealing with analysis of flows of information and survey-analytical work. Such information helps obtain a bearing on the flows of records, assess the significance of information and, to some extent, determine the prospects of development of a problem being worked on by a specific team.

The reference books of several institutes [3, 4, 8] list the scientific personnel of laboratories (laboratory head, senior and junior scientific workers), but in most such books information is given only about laboratory heads [13-14, 17-19], whereas no information about scientific personnel is given at all in some reference books [21], which makes informal inter-institute contacts difficult.

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Table 1. Reference books of biological institutes of USSR Academy of Sciences and Union republic academies

Publishing organization and title of reference book	Historical essay(intro)	Information about management personnel	Information about scientific personnel	Sci.departments: main directions of sci.res.	Sci.departments: main results of sci. research	Sci.departments: long-term plan of development	list of main publications
Inst.Developmental Biol. "Brief Reference Book" [3]	+	Director Deputy dir. Sci.secret. Inst.address	Lab hd. Sr sci. Jr sci.	+	+	-	-
Institute of Protein, "Brief Information: [4]	+	Director Deputy dir. Sci. secr. Address	Lab hd. Sr sci. Hr sci.	+	+	-	-
Inst. General Genetics, "Brief Reference Book" [5]	+	Director Deputy dir. Sci.secr. Address	Lab hd. [head]	+	+	+	+
Inst.Molec.Biology [6]	+	Director	Lab hd., group leaders	+	+	-	+
Inst.Plant Physiology [7]	+	Director	Lab hd.	+	+	for some labs	+
Inst.Evolution.Morph. & Ecology of Animals [8]	+	Director Deputy dir. Sci.secr. Address	Lab hd. Sr sci. Jr sci.	+	+	-	+
Institute of Physiology, Kiev [9]	+	Director	Lab hd.	+	+	-	+
Institute of Biochemistry [10]	+	Director	Lab hd. Authors of cit. works	+	+	for some labs	+
Inst.Botany imeni N. G. Kholodnyy [11]	+	Director	Lab hd. Staff	+	+	-	+
Inst. of Physiology, Yerevan [12]	+	Director	Lab hd. Authors of cit. works	+	+	+	+
Inst.Cytol. and Genetics, "Brief Reference Book" [13]	+	Director Deputy dir. Sci. secr. Chief engineer	Lab hd.	+	+	-	+

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Table 1. (continued)

Inst. of Microbiology, "Prospectus" [14]	+	Director	Lab hd.	+	+	-	+
Inst. of Photosynthesis, "Prospectus" [15]	+	Director Address	Lab hd., Group leaders	+	+	-	-
Inst. of Photosynthesis, "Brief Information" [16]	+	Director	Lab hd. Group leaders	+	+	-	-
Inst. Experim. Plant Biol., [17]	+	Director	Lab hd.	+	+	-	+
Institute of Zoology [18]	+	Director Deputy dir. Sci.secret. Address	Dept hds.	+	+	-	-
Institute of Botany, Tashkent [19]	+	Director	Dept hds.	+	+	-	+
Inst. Physiology, Novosibirsk, "Brief Reference Book," [20]	+	Director Deputy dir. Sci.secr.	Lab hd. Group leader Sr Sci.	+	+	-	+
Inst.Protein Research, "Prospectus," [21]	+	Director Address	-	+	+	-	+

Most of the reference books analyzed had the following structure: 1) introduction (historical essay); 2) information about scientific research activity of different laboratories; 3) information about the work of general institute departments (experimental stations, libraries, etc.); 4) main publications of the institute (see Table 1).

The introduction usually sheds brief light on the history of establishment and development of the institute, main problems and directions of scientific research at the institute, the most important achievements of scientific research, scientific and public activities of the institute, introduction of results of SR [scientific research] in the national economy, international scientific ties. As we have indicated above, information about management and the administrative body of the institute is also given in the introduction in most reference books.

Information about SR in laboratories (departments) is the main part of the reference books. There is a logical order of laboratories described, and in some cases it is explained in the introduction, while in others it is easy to comprehend from the meaning. Grouping laboratories according to similarity of projects worked on is the most informative, and for the users the most convenient presentation is to have problems that are worked on by several laboratories listed in separate headings [10, 13].

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When preparing reference books for publication, special attention should be given to heading titles, which reflect meaning and make the presentation orderly, clear and understandable [25, 26], and also activates the reader's attention, accelerating the process of transmitting information [27].

In most of the reference books we analyzed, the main objectives of scientific research activity in all scientific and scientific-engineering departments of the institute are reflected distinctly and rather briefly; there is indication of the objects and methods of investigation, main achievements of SR. However, in some reference books [6, 10], very detailed and expanded information is given about SR; the books are oversaturated with terminology. Superfluous details, like superfluous brevity, are equally detrimental to informativeness of the reference books. The degree to which the information is condensed should depend on the object to which it addresses itself [25, 26].

The reference books of some institutes contain information about scientific-engineering departments and services [3-5], international scientific ties, introduction of scientific achievements in the national economy [19] and experimental collections [14].

In some manuals [5, 7, 10, 12], there is information about the prospects of development of SR, and in some cases these are long-term forecasts (in the manual of the Institute of General Genetics are given the long-term plans for development of laboratory projects over a 25-year period: 1974 to 1999); occasionally [12], the plan for SR development covers a 5-year period; in some cases [7, 10], plans for future research at some laboratories are described without indication of target dates. Such information is of interest both to scientists and information workers; they aid in coordinating research, establishing contacts, and they point to the possible routes of information retrieval. Long-term forecasts are also of interest because they are made with consideration of development of the ideas and methods of research, as well as possible appearance of major discoveries in a given or related branch of science.

In some reference books, at the end of the book or after the information about individual laboratories, there is a list of the main publications of the staff of an institute or laboratory. These bibliographies include both major publications of institute staff members (monographs, collections, textbooks) and articles in periodicals, and even papers and summaries of papers submitted for publication [13]. In anniversary editions of reference books [6, 10], there are extensive bibliographies (monographs, collections, textbooks and educational aids, popular scientific pamphlets, surveys, author certificates, etc.), starting at the time the institute was founded. They are usually listed in the guides of institutes that do not publish either bibliographies or bibliographic-abstract collections. When compiling a bibliography of the main publications, some manuals do not take into consideration the timeliness of some work or other and obsolescence of information contained in it. Evidently, it is desirable to list the main publications in the reference book only if the institute does not publish bibliographic abstract publications regularly.

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Most of the reference books analyzed are 45-70 pages in length. Of course, the size of such a manual depends on the rank of the institute, number of laboratories and scientific-technical departments. If the size is larger, due to superfluous information (which could be very interesting but not essential to the reference book), it is difficult to use these publications as institute guides. Quite often, the size of a reference book is increased by inclusion of photographs, which are usually not very informative and of poor quality.

For the sake of comparison to reference books published by Soviet institutes, we analyzed two reference books of foreign institutes: the one of the Japanese Institute of Genetics [28] and Hubrecht Laboratory of the International Embryological Institute [29]. The information in the guide of the Japanese Institute of Genetics is given in the following order: location of the institute with indication of means of transportation; brief essay on foundation and development of the institute, administrative-executive apparatus and scientific personnel, scientific-technical and ancillary departments, scientific departments (main problems and results of SR in laboratory departments), periodical publications of the institute (annual bibliographic-abstract collection). In addition, some very important information is given in this guide about experimental collections at the institute (bacterial strains, mutations of drosophila, strains and mutant stock of laboratory animals, breeds, varieties, mutants of plants).

In the reference book published by the Hubrecht Laboratory, there are data about the status and objectives of the laboratory, brief historical information about it, location of different departments, structure of the laboratory, administrative and scientific personnel, topics studied by scientific departments, international programs of SR, working conditions in the laboratory for foreign scientists. There is a detailed description of the central embryological collection, information service, scientific library and reproduction of scientific materials. There is a brief summary in this book, in German and French, it serves as a good guide to the laboratory and really takes into consideration the information needed by foreign scientists visiting this laboratory.

The knowhow of foreign institutes can also be adopted in Soviet practice. Evidently, for us the most valuable factor is to take into consideration the information needs of specialists who wish to learn about an institute and establish personal contacts. Expressly such information is least reflected in Soviet reference books. At the same time, there is much more thorough and distinct coverage of scientific research activities at the institutes in the Soviet guides. Adoption of foreign knowhow to publication of Soviet reference books would improve the quality of these publications, which are important to institutes, as well as their informativeness, relevance and communicative role.

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Continuing Bibliographic-Abstract Publications

Publication of bibliographic-abstract collections is practiced both in the USSR and abroad; in them, emphasis is laid on the results of SR activities of institutes within a specific, usually short, period of time. As a rule the bibliographic-abstract publications are continuing editions, mostly annual. These publications are useful in the following respects: 1) they permit rapid familiarization with the results and status of SR, not only of individual scientists, but the entire scientific team of an institute; 2) they publicize SR achievements of the institute; 3) there is less loss of needed information related to scattering of publications; 4) they help establish scientific contacts; 5) they help single out author teams.

We analyzed the continuing bibliographic-abstract publications of eight Soviet and five foreign biological institutes.

In the last few years, several Soviet institutes have published annual bibliographic-abstract collections under various titles: "Results of Scientific Work," "Results of Scientific and Scientific Administrative Activity," "Abstracted Information About Completed Works," "Abstracts of Scientific Research Papers," "List of Publications on the Problem of....," etc., i.e., the titles of the annuals, like those of the reference books, are quite diverse [30-37] (Table 2).

In some of the collections we scrutinized, the main part is the introduction, in which there is a brief description of the structure of the institute and main directions of its work, as well as the principle of classification of abstracted information and extent to which it is complete.

The annotation to the collection plays the role of an introduction in the annual of the Institute of Cytology and Genetics, Siberian Department of USSR AS [Academy of Sciences] [32]. There is no introduction in the collections of abstracts of the Institute of Microbiology and Virology imeni D. K. Zabolotnyy [34], Institute of Photobiology [31] and Siberian Institute of Plant Physiology and Biochemistry [37]. This makes it difficult to retrieve and classify information, as well as to single out the main directions of activities of an institute.

The collection published by the Institute of Marine Biology, Far East Research Center, USSR AS [36], contains rather comprehensive information about the history of establishment of the institute, its structure, administrative-management and scientific personnel, as well as a general description of directions and results of SR conducted in different laboratories, i.e., information that is usually contained in reference books. Evidently, annual repetition of such information is hardly expedient, and inclusion thereof in the annual is related, apparently, in this case to the fact that this institute does not publish a specialized reference book.

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Table 2. Bibliographic-abstract and abstract publications of biological institutes of the USSR

Publishing organization	(1)	(2)	(3)	(4) (5)	(4) (6)	(4) (7)	References
Institute of Developmental Biology. "Results of Scientific Work" [30]	+	Accord. to structural departments of institute	Published	+	+	+	All published works. Alphabetical author index
Inst. Photobiology, "List of Publications on Photosynthesis"[31]	-	Alphabetical author index	Published	+	-	+	-
Inst. Cytology & Genetics, "Results of Scientific Work," "Problems of Theoretical and Applied Genetics" [32]	+	According to direction of SR	Main unpublished works	+	-	-	Classified according to structural departments of institute. List of main public.
Inst. of Biology, Minsk, "Abstracts of SR Works" [33]	+	According to structural departments of institute	Unpublished works, in press	+	-	-	Classified accord. to labs and alphabetical author index. List of all published works
Inst.Microbiol. & Virol., "Abstracted Information About Completed SR," "SR Abstracts" [34]	-	According to directions of SR	Completed published & unpublished works	+	+	--	-
Inst. Plant & Animal Ecology, Ural Research Center, USSR AS, "Problems of Genetics and Breeding in the Urals" (informative data) [35]	+	According to directions of SR	Published & unpublished works	+	-	-	-
Inst. Marine Biol., USSR AS, Far East Research Center "Scientific Reports" [36]	+	According to directions of SR	Published & unpublished works	+	-	-	Alphabetical list of all published works
Siberian Inst. Physiol. & Biochem. Siber.Branch USSR AS, "Current Information" [37]	-	According to	Not known	+	-	-	-

Key: 1) introduction
2) method of classifying information
3) works abstracted
4) form of condensing information
5) monographic abstract
6) survey abstract
7) annotatiom

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Most of the abstract and bibliographic-abstract publications cover information about SR activities of an institute over a short period of time. In Soviet annuals, the monographic abstract is the main form of condensing information, less often there are survey abstracts and annotations. Inclusion in abstract publications of the results of unpublished works (works submitted or prepared for publication) increases the currentness and timeliness of the information.

In the annuals of the Institute of Developmental Biology, USSR AS (IDB) [30] and Institute of Photobiology [31], only published works are abstracted; in the annuals of IDB, there are mainly survey abstracts and in those of the Institute of Photobiology, only monographic abstracts. In the annuals of the Institute of Cytology and Genetics [32] and Institute of Biology [33], there are abstracts only of unpublished works; in those of the Institute of Biology there is indication of where the abstracted work will be published. There are no abstracts for published works.

Both published and unpublished works are abstracted in the annuals of the Institute of Microbiology and Virology [34], Institute of Plant and Animal Ecology [35] and Institute of Marine Biology [36]. The annual of the Siberian Institute of Plant Physiology and Biochemistry indicates whether the abstracted works were published or not.

As a rule, the annuals abstract articles from journals and collections, and they have annotations for surveys and monographs. In each instance, the question of abstracting or annotating a work, or merely including it in a list of publications, is decided on an individual basis.

Special mention should be made of the inclusion in the annuals of proceedings of conferences, symposiums and congresses. According to information of UNESCO [38], proceedings of almost half of all conferences are published only in the form of brief preliminary reports (summaries of papers), over half the papers published in "proceedings of conferences, etc.," are not published in other sources, for example periodicals [39]. The question of loss of information reported at conferences, congresses and symposiums is a very acute one. Abstracting or at least annotation of such papers in annuals could reduce somewhat the loss of such valuable information.

Some institutes [31, 34, 35, 37] published abstract collections, in which there are no lists of published works. The informative value of such publications is considerably lower than that of bibliographic-abstract editions, since they do not facilitate retrieval of information.

The abstracts and annotations in annuals of most institutes are classified according to the subject orientation of SR and objects of investigations. In only one of the abstract collections [31] the abstracts are listed in alphabetical order (according to authors' names), and a bibliographic description of the work precedes each abstract. There is no introduction, separate list of publications or any other index in this collection. For

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this reason, in spite of the fact that the abstracts and annotations in this collection are very competently prepared, and there is also an English version thereof, the collection is not convenient for users of information: the extent to which institute publications are covered in the collection is not apparent. It is difficult to single out the achievements referable to individual scientific research directions of the institute, and the entire collection must be leafed through to retrieve required information.

"The List of Classification Headings in the Main Information Publications of the USSR" [40] is an example of systematization of scientific information. It is based on classification of information in accordance with the hierarchic structure of a specific branch of science. The information publications of institutes by no means presume to be universal and complete to the extent of main information editions; however, the principle of classification of information, which has been developed for the main information publications, can also be used for the bibliographic-abstract publications of institutes, and the information should not be classified according to the structure of some branches of science, but according to the directions of scientific research being developed at an institute.

One of the most important parts of bibliographic-abstract publications is a list of published works. As a rule, the list is compiled in alphabetical order of authors; occasionally it is classified according to problems or structural departments of institutes.

Seldom is use made of ancillary indexes in annuals [30]. However, it may be assumed that with further refinement of the structure of annuals proper attention will be given to them.

Since annual abstract and bibliographic-abstract collections of many Soviet biological institutes began to be published recently, we still do not have standardized rules for compilation thereof, screening information and forms of condensation. It is imperative to investigate the flow of information from institutes, the information requirements of different categories of scientific workers and management of institutes, as well as the many years of experience gained by foreign biological institutes in publishing analogous annuals.

We analyzed the annuals of five foreign biological institutes. The annual bibliographic-abstract publications of foreign biological institutes have the functional purpose of institute reports about scientific research work. This is reflected in the titles of some of the annuals: "Annual Report," "Scientific Report," etc. The functions of such bibliographic-abstract publications are close to the functions of annual reports of foreign companies [41].

The structure of annuals of foreign biological institutes is stereotyped. First there is brief information about the structure of the institute, administrative and scientific personnel, trustees and consultant councils,

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foreign trainees and international scientific ties. Special attention is given to the results of SR. There is usually a list of published works at the end.

In the annuals of the Strangeways Laboratory (Cambridge, Great Britain) [42], which consist of six scientific sections, information is given annually only about three completed scientific research projects (one per department). Review papers (in the form of expanded survey abstracts) of three members of the laboratory staff are prepared on the basis of data both from works published in the reported year, and unpublished works. The topics of studies of other members of the laboratory staff are only mentioned. The list of publications includes articles and brief reports of all members of the laboratory staff.

In annuals published by the Laboratory of Molecular Embryology (Italy) [24] there is annotation or abstracting of all published articles and those prepared for publication. Monographic abstracts are given for some of the articles that are considered the most important in the opinion of the annual compilers, while annotations are provided for other works. The abstracts and annotations are not accompanied by references to bibliographies, which makes it difficult to use this annual for retrieval of information.

In the annuals of the Institute of Embryology and Experimental Teratology (France) [43], there are monographic and survey abstracts and annotations for published and unpublished works. The abstracts and annotations are accompanied by references to a bibliography, which includes articles from periodicals, collections and monographs. There is a special listing of survey and popular science articles.

In the annual of the Institute of Animal Genetics (Great Britain) [44], which covers a 4-year period of institute activities, information about SR is given in the form of survey abstracts, mainly of works published in this period, and they are grouped according to problems and objects of research. This form of condensing information, with a distinct heading classification, makes it possible to obtain a rather complete idea about the status of a problem, spending the least amount of time on reading. In the text of the abstracts there are references to both published works (articles in periodicals, in collections, monographs, papers delivered at conferences) and those submitted for publication (with indication of the journal to which the work was submitted). Bibliographies are compiled according to different laboratories.

In the annual of the Embryology Department of Carnegie Institution (United States) [45], information about SR is submitted in the form of reports, which are based on survey abstracts of both published and unpublished, completed works. Expanded abstracts, with graphs, tables, diagrams, photographs and figures, are furnished for studies in which much experimental material is submitted on a completed research project, or an original solution is given for pressing problems with indication of routes of future

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research. The list of publications includes articles from periodicals, collections, monographs and papers delivered at conferences, etc.

Monographic abstracts of published and unpublished works, which are classified according to objects of investigation and direction of SR, are given in the annuals of the Hubrecht Laboratory of the International Embryological Institute [46]. There is an alphabetical index of published works and those prepared for publication.

Thus, along with some differences, there are also some common features in annuals of foreign and Soviet institutes. Current information is included in both Soviet and foreign annuals. Both abroad and in Soviet practice, the abstract is the main form of condensing information, and the survey abstract is used the most often.

Abstracted information in foreign annuals is given along with data about the structure of an institute and its scientific personnel. This plays an important role in evaluating information, when one needs to know not only what is reported, but who did the work and under whose supervision it was done.

Information about participation of institute staff members at congresses, conferences and symposiums is important. As a rule, such information is included in foreign annuals and very rarely in Soviet ones.

Thus, analysis of bibliographic-abstract publications revealed that, along with features in common, they are characterized by diversity of structure, nature of information and form of condensation thereof, differences in approach to classification of information. Determination of the most reasonable forms of transmitting information is one of the first steps toward upgrading these publications.

Conclusions

1. The reference-information and bibliographic-abstract publications of biological scientific research institutes play an important role in development of scientific communication, expediting exchange of information about the results of scientific research conducted by large scientific groups, determination of the routes for retrieval of information; they aid in coordinating scientific research and in analytical-survey work. The information contained in such publications is intended both for scientific workers and information workers, as well as the administrative-management body of the institutes. For this reason, we are faced with the pressing problem of upgrading these publications, optimizing and standardizing their structure, clearly defining their functional and goal-oriented purpose.

2. The chief purpose of reference and information publications is to aid in establishing scientific contacts, to serve as guides for institutes. This must be reflected in the structure and appropriate screening of

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information: attention should be directed chiefly to information about the administrative-management body of the institutes, structure of an institute and its scientific personnel. Information about an institute's scientific research activities should be more general, so that the information would be relevant for a long period of time and readily accessible to a wide circle of specialists.

3. The main function of bibliographic-abstract publications is to provide current information about the results of scientific research done at an institute within a relatively short period of time. For such publications, the best form of condensing information is the survey abstract. The best form of classifying information is according to the directions of SR activity of the institute. The bibliography of publications by the staff of an institute is the most important part of such publications; if it is complete, the annuals can be used in many aspects, there will be less loss of information and faster retrieval thereof.

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